

Claims

1. Use of an antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof specifically binds to an integrin alpha10 polypeptide, in the manufacture of a medicament for the treatment of an aggressive cancer form selected from the group consisting of aggressive breast cancer, aggressive lung cancer, aggressive prostate cancer and aggressive pancreatic cancer, or a metastasis of any one of said cancer forms.
2. The use according to claim 1, wherein the aggressive breast cancer is selected from the group consisting of triple negative breast cancer and inflammatory breast cancer; and/or

wherein the triple negative breast cancer is selected from the group consisting of basal-like 1 breast cancer, basal-like 2 breast cancer, claudin-low breast cancer, metaplastic breast cancer (MBC), interferon-rich breast cancer, immunomodulatory breast cancer, mesenchymal breast cancer, mesenchymal stem-like breast cancer, luminal androgen receptor breast cancer and unstable breast cancer; and/or

wherein the aggressive lung cancer is selected from the group consisting of squamous cell lung carcinoma, lung adenocarcinoma, large cell lung carcinoma and small-cell lung carcinoma; and/or

wherein the aggressive prostate cancer is small cell neuroendocrine carcinoma (SCNC); and/or

wherein the aggressive pancreatic cancer is a neuroendocrine tumor; and/or

wherein the aggressive pancreatic cancer and/or neuroendocrine tumor of the pancreas is a grade I, grade II or grade III pancreatic cancer.
3. The use according to claim 1 or claim 2, wherein the integrin alpha10 polypeptide is expressed on the surface of a malignant cell and/or a tumor-associated cell.
4. The use according to any one of the preceding claims, wherein the antibody is a monoclonal antibody, polyclonal antibody, a chimeric antibody, a single chain antibody or fragment thereof; such as

wherein the antibody is a non-human antibody, a chimeric antibody, a bispecific antibody, a humanized antibody or a human antibody; such as
 wherein the antibody is a mouse monoclonal antibody; such as
 wherein the antibody is a human monoclonal antibody.

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5. The use according to any one of the preceding claims, wherein the antibody is:
 a) a monoclonal antibody, produced by the hybridoma cell line deposited at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH under the accession number DSM ACC2583; or

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b) an antibody which competes for binding to the same epitope as the epitope bound by the monoclonal antibody produced by the hybridoma deposited at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH under the accession number DSM ACC2583; or

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c) a fragment of a) or b), wherein said fragment is capable of binding specifically to the extracellular I-domain of the integrin $\alpha 10$ polypeptide chain.

6. The use according to any one of the preceding claims, wherein the antibody or antigen binding fragment comprises:

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a heavy chain variable region comprising

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- a. a CDR-H1 comprising or consisting of the amino acid sequence of SEQ ID NO: 4;
- b. a CDR-H2 comprising or consisting of the amino acid sequence of SEQ ID NO: 5; and
- c. a CDR-H3 comprising or consisting of the amino acid sequence of SEQ ID NO: 6;

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and

a light chain variable region comprising

- d. a CDR-L1 comprising or consisting of the amino acid sequence of SEQ ID NO: 7;
- e. a CDR-L2 comprising or consisting of the amino acid sequence of SEQ ID NO: 8; and
- 5 f. a CDR-L3 comprising or consisting of the amino acid sequence of SEQ ID NO: 9.

or a variant of any one of SEQ ID NO:s 4 to 9, wherein any one amino acid has been altered for another amino acid, with the proviso that no more than 3 amino acids have been so altered, for example wherein 2, or 1 amino acids have been so altered; such as

wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 10; such as

15 wherein the antibody or antigen-binding fragment comprises a light chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 11.

7. The use according to any one of the preceding claims, wherein the antibody or antigen-binding fragment thereof is conjugated to an additional moiety, such as

20 wherein the additional moiety comprises a detectable moiety, such as a detectable moiety selected from the group consisting of a fluorophore, an enzyme and a radioactive tracer or radioisotope.

8. The use according to any one of the preceding claims, wherein the antibody or antigen-binding fragment thereof is conjugated to an additional moiety, such as

25 wherein the additional moiety comprises a cytotoxic moiety; such as

wherein the cytotoxic moiety is selected from a group consisting of a toxin, a chemotherapeutic agent and a radioactive agent, or combinations thereof; such as

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wherein said toxin is selected from the group selected from microtubule toxins, DNA toxins and transcription toxins; such as

wherein said microtubule toxins are selected from the group consisting of Auristatin-based toxins, Maytansinoid-based toxins, Tubulysins-based toxins and Eribulin; such as

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wherein said transcription toxin is an RNA polymerase II inhibiting agent;
such as

wherein said transcription toxin is selected from the group consisting of
Doxorubicin, Doxorubicin derivatives and Amanitin; such as

5 wherein the transcription toxin is selected from the group consisting of
shiga and shiga-like toxins; type I ribosome inactivating proteins, type II ribosome
inactivating proteins and saporin, or combinations thereof; such as

wherein the type I ribosome inactivating protein is trichosanthin and/or
luffin; such as

10 wherein the type II ribosome inactivating protein is ricin, agglutinin and/or
abrin.

9. The use according to any one of the preceding claims, wherein the antibody or
antigen-binding fragment thereof is capable of inducing cell death and/or
15 inhibiting growth and/or inhibiting proliferation and/or inhibiting migration of cells
expressing an integrin alpha10 polypeptide.

10. The use according to claim 9, wherein the cells are malignant cells and/or tumor-
associated cells, such as
20 wherein the malignant cells or tumor-associated cells are cancer
associated fibroblast (CAFs), stromal cells, stem cells and/or stem-like cells.

11. The use according to any one of the preceding claims, wherein the integrin
alpha10 polypeptide is a part of an integrin alpha10 beta1 heterodimer.

25 12. An in vitro method for detecting an aggressive cancer cell in a subject, said
method comprising the steps of:

- a. providing a sample of a tissue suspected of comprising cancer cells of the
subject;
- 30 b. optionally analyzing in the sample of the tissue the presence of one or more
cells having a cancer morphology,
- c. analyzing in the tissue the presence of an antigen comprising an integrin
alpha10 polypeptide or a fragment thereof,
- d. optionally determining the expression level of the integrin alpha10 antigen,

wherein presence of one or more cells having a cancer morphology in combination with expression of integrin alpha10 antigen are indicative of the presence of an aggressive cancer form in the subject, and wherein said aggressive cancer form is selected from the group consisting of aggressive breast cancer, aggressive lung cancer, aggressive prostate cancer and aggressive pancreatic cancer, or a metastasis of any one of said aggressive cancer forms.

13. An in vitro method for diagnosis of an aggressive cancer form in a subject, the method comprising the steps of:
 - a. providing a sample of a tissue suspected of comprising cancer cells of the subject;
 - b. optionally analyzing in the sample of the tissue the presence of one or more cells having a cancer morphology;
 - c. analyzing in the sample of the tissue the presence of an antigen comprising an integrin alpha10 polypeptide or a fragment thereof,
 - d. optionally determining the expression level of the integrin alpha10 antigen, and

wherein presence of one or more cells having a cancer morphology in combination with expression of integrin alpha10 antigen are indicative of the presence of an aggressive cancer form in a sample, wherein said aggressive cancer form is selected from the group consisting of aggressive breast cancer, aggressive lung cancer, aggressive prostate cancer and aggressive pancreatic cancer, or a metastasis of any one of said aggressive cancer forms, thereby diagnosing an aggressive cancer form in a subject.

14. An in vitro method for classification of a triple negative breast cancer tumor sample of a subject, said method comprising:
 - a. providing a sample of a breast tissue suspected of comprising cancer cells of the subject;
 - b. isolating breast cancer cells characterized as being ER negative, PR negative and HER2 negative;
 - c. determining in the isolated cells an expression level of an antigen comprising an integrin alpha10 polypeptide or a fragment thereof, and

- d. comparing the expression level determined in c. to a control level, wherein said control level is the average expression level of the antigen observed in healthy and/or benign breast tissue;
 wherein an expression level of the antigen in the breast cancer cells higher than a control level, and an expression status of ER negative, PR negative and HER2 negative are indicative of a basal-like triple negative breast cancer or a luminal triple negative breast cancer,
 thereby classifying the triple negative breast cancer tumor sample as belonging to a basal-like triple negative breast cancer tumor or to a luminal triple negative breast cancer tumor.
15. An in vitro method for determining a prognosis for an aggressive cancer form for a subject, the method comprising:
 - a. providing a sample of a cancer tumor tissue of the subject;
 - b. optionally analyzing in the sample of the tissue the presence of one or more cells having a cancer morphology;
 - c. analyzing in the sample of the tissue the presence of an antigen comprising an integrin alpha10 polypeptide or a fragment thereof,
 - d. optionally determining the expression level of the integrin alpha10 antigen, and comparing the determined expression level to a control level, wherein the control level is the average expression level of the antigen observed in healthy and/or benign tissue of the same tissue type as the sample;
 - e. determining an unfavorable prognosis of the aggressive cancer form when one or more cells having a cancer morphology are present in the sample of the tissue in combination with expression of the integrin alpha10 antigen, and/or
 the expression level of the integrin alpha10 antigen is higher than the control level,
 wherein the aggressive cancer form selected from the group consisting of aggressive breast cancer, aggressive lung cancer, aggressive prostate cancer and aggressive pancreatic cancer, or a metastasis of any one of said aggressive cancer forms.

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16. Use of a therapeutically effective amount of an antibody or antigen-binding fragment thereof, wherein the antibody is specific for integrin alpha10 polypeptide, in the manufacture of a medicament for the prevention of metastasis from a primary aggressive cancer selected from the group consisting of aggressive breast cancer, aggressive lung cancer, aggressive prostate cancer and aggressive pancreatic cancer.
 17. The use according to claim 16 wherein the antibody or antigen-binding fragment is provided for administration upon detection of the primary cancer.